

# Abdominal Height Accurately Gauges Adiposity

BY FRAN LOWRY

Orlando Bureau

**NEW ORLEANS** — In a patient with a body mass index of 40 kg/m<sup>2</sup> or more, measuring the height of the abdomen while the patient is lying down is a better indicator of visceral adiposity than is measuring waist circumference, according to a poster presentation at the annual meeting of NAASO, the Obesity Society.

In fact, said Dr. Nana Gletsu Miller,

measuring waist circumference in such individuals is difficult, impractical, and does not provide a good measure of intra-abdominal fat stores, which is the fat that is more detrimental to health.

Dr. Gletsu Miller, of Emory University, Atlanta, showed measuring sagittal abdominal diameter while patients were in a supine position provided information that was more predictive of changes in insulin resistance and other cardiometabolic risk factors during weight loss than did waist circumference measured when the patient was standing up.

The 30 severely obese female patients were assessed at baseline, 1 month, and 6 months after Roux-en-Y gastric bypass or adjustable banding surgery for weight loss.

Fifteen of the women also were assessed at 24 months postsurgery.

Visceral and subcutaneous adipose tissue volumes were determined using computed tomography. The height of the abdominal region was measured with a sliding-beam caliper, and waist circumference was measured at the iliac crest with a tape measure.

Other measures included hepatic insulin sensitivity, which was determined using the homeostatic model assessment of insulin resistance index that measures fasting glucose and insulin concentrations, along with the following indicators of cardiometabolic risk: systolic blood pressure, fasting LDL cholesterol, triglycerides, and high-sensitivity C-reactive protein.

All of the subjects exhibited significant decreases in general and abdominal adiposity, sagittal abdominal diameter, waist circumference, and visceral and subcutaneous fat volumes. They also improved measures of cardiometabolic risk, Dr. Gletsu Miller said.

However, as the severely obese subjects experienced weight loss over 6 months, changes in sagittal abdominal diameter accounted for 15% of the changes in intra-abdominal fat volumes, whereas changes in waist circumference did not significantly explain these changes, she said.

Dr. Gletsu Miller said more studies need to be done to determine a cutoff value that will best predict insulin resistance and other risk factors in severely obese patients. ■

## LEXAPRO® (escitalopram oxalate) TABLETS/ORAL SOLUTION

(3% and <1%); Anorgasmia\* (2% and <1%); \*Events reported by at least 2% of patients treated with Lexapro are reported, except for the following events which had an incidence on placebo: Lexapro: headache, upper respiratory tract infection, back pain, pharyngitis, inflamed injury, anxiety; \*Primarily ejaculatory delay. †Denominator used was for males only (N=225 Lexapro; N=188 placebo). ‡Denominator used was for females only (N=490 Lexapro; N=404 placebo). **Generalized Anxiety Disorder Table 3** enumerates the incidence, rounded to the nearest percent of treatment-emergent adverse events that occurred among 429 GAD patients who received Lexapro 10 to 20 mg/day in placebo-controlled trials. Events included are those occurring in 2% or more of patients treated with Lexapro and for which the incidence in patients treated with Lexapro was greater than the incidence in placebo-treated patients. The most commonly observed adverse events in Lexapro patients (incidence of approximately 5% or greater and approximately twice the incidence in placebo patients) were nausea, ejaculation disorder (primarily ejaculatory delay), insomnia, fatigue, decreased libido, and anorgasmia (see TABLE 3). **TABLE 3: Treatment-Emergent Adverse Events: Incidence in Placebo-Controlled Clinical Trials for Generalized Anxiety Disorder (Lexapro (N=429) and Placebo (N=427)).** **Autonomic Nervous System Disorders:** Dry Mouth (9% and 5%), Sweating Increased (4% and 1%), Central & Peripheral Nervous System Disorders: Headache (24% and 17%), Paresthesia (2% and 1%), **Gastrointestinal Disorders:** Nausea (18% and 8%), Diarrhea (8% and 6%), Constipation (5% and 4%), Indigestion (3% and 2%), Vomiting (3% and 1%), Abdominal Pain (2% and 1%), Flatulence (2% and 1%), Toothache (2% and 0%), **General:** Fatigue (8% and 2%), Influenza-like symptoms (5% and 4%), **Musculoskeletal:** Neck/Shoulder Pain (3% and 1%), **Psychiatric Disorders:** Somnolence (13% and 7%), Insomnia (12% and 6%), Libido Decreased (7% and 2%), Dreaming Abnormal (3% and 2%), Appetite Decreased (3% and 1%), Lethargy (3% and 1%), Yawning (2% and 1%), **Urogenital:** Ejaculation Disorder<sup>†‡</sup> (14% and 2%), Anorgasmia\* (6% and <1%), Menstrual Disorder (2% and 1%). \*Events reported by at least 2% of patients treated with Lexapro are reported, except for the following events which had an incidence on placebo: Lexapro: inflamed injury, dizziness, back pain, upper respiratory tract infection, rhinitis, pharyngitis. †Primarily ejaculatory delay. ‡Denominator used was for males only (N=182 Lexapro; N=195 placebo). †Denominator used was for females only (N=247 Lexapro; N=232 placebo). **Dose Dependency of Adverse Events** The potential dose dependency of common adverse events (defined as an incidence rate of ≥5% in either the 10 mg or 20 mg Lexapro groups) was examined on the basis of the combined incidence of adverse events in two fixed-dose trials. The overall incidence rates of adverse events in 10 mg Lexapro-treated patients (66%) was similar to that of the placebo-treated patients (61%), while the incidence rate in 20 mg/day Lexapro-treated patients was greater (86%). **Table 4** shows common adverse events that occurred in the 20 mg/day Lexapro group with an incidence that was approximately twice that of the 10 mg/day Lexapro group and approximately twice that of the placebo group. **TABLE 4: Incidence of Common Adverse Events\* in Patients with Major Depressive Disorder Receiving Placebo (N=311), 10 mg/day Lexapro (N=310), 20 mg/day Lexapro (N=252);** Insomnia (4%, 7%, 14%); Diarrhea (5%, 6%, 14%); Dry Mouth (3%, 4%, 9%); Somnolence (1%, 4%, 9%); Dizziness (2%, 4%, 7%); Sweating Increased (<1%, 3%, 8%); Constipation (1%, 3%, 6%); Fatigue (2%, 2%, 6%); Indigestion (1%, 2%, 6%); Adverse events with an incidence rate of at least 5% in either of the Lexapro groups and with an incidence rate in the 20 mg/day Lexapro group that was approximately twice that of the 10 mg/day Lexapro group and the placebo group. **Male and Female Sexual Dysfunction with SSRIs** Although changes in sexual desire, sexual performance, and sexual satisfaction often occur as manifestations of a psychiatric disorder, they may also be a consequence of pharmacologic treatment. In particular, some evidence suggests that SSRIs can cause such untoward sexual experiences. Reliable estimates of the incidence and severity of untoward experiences involving sexual desire, performance, and satisfaction are difficult to obtain, however, in part because patients and physicians may be reluctant to discuss them. Accordingly, estimates of the incidence of untoward sexual experience and performance cited in product labeling are likely to underestimate their actual incidence. **Table 5** shows the incidence rates of sexual side effects in patients with major depressive disorder and GAD in placebo-controlled trials. **TABLE 5: Incidence of Sexual Side Effects in Placebo-Controlled Clinical Trials (In Males Only: Lexapro (N=407) and Placebo (N=383));** Ejaculation Disorder (primarily ejaculatory delay) (12% and 1%); Libido Decreased (6% and 2%); Impotence (2% and <1%). (In Females Only: Lexapro (N=373) and Placebo (N=636)); Libido Decreased (3% and 1%); Anorgasmia (3% and <1%) There are no adequately designed studies examining sexual dysfunction with escitalopram treatment. Priligis has been reported with all SSRIs. While it is difficult to know the precise risk of sexual dysfunction associated with the use of SSRIs, physicians should routinely inquire about such possible side effects. **Vital Sign Changes** Lexapro and placebo groups were compared with respect to (1) mean change from baseline in vital signs (pulse, systolic blood pressure, and diastolic blood pressure) and (2) the incidence of patients meeting criteria for potentially clinically significant changes from baseline in these variables. These analyses did not reveal any clinically important changes in vital signs associated with Lexapro treatment. In addition, a comparison of supine and standing vital sign measures in subjects receiving Lexapro indicated that Lexapro treatment is not associated with orthostatic changes. **Weight Changes** Patients treated with Lexapro in controlled trials did not differ from placebo-treated patients with regard to clinically important change in body weight. **Laboratory Changes** Lexapro and placebo groups were compared with respect to (1) mean change from baseline in various serum chemistry, hematology, and urinalysis variables, and (2) the incidence of patients meeting criteria for potentially clinically significant changes from baseline in these variables. These analyses revealed no clinically important changes in laboratory test parameters associated with Lexapro treatment. **ECG Changes** Electrocardiograms from Lexapro (N=625), racemic citalopram (N=351), and placebo (N=527) groups were compared with respect to (1) mean change from baseline in various ECG parameters and (2) the incidence of patients meeting criteria for potentially clinically significant changes from baseline in these variables. These analyses revealed (1) a decrease in heart rate of 2.2 bpm for Lexapro and 2.2 bpm for racemic citalopram, compared to an increase of 0.3 bpm for placebo and (2) an increase in QTc interval of 3.9 msec for Lexapro and 3.7 msec for racemic citalopram, compared to 0.5 msec for placebo. Neither Lexapro nor racemic citalopram were associated with the development of clinically significant ECG abnormalities. **Other Events Observed During the Premarketing Evaluation of Lexapro** Following is a list of WHO terms that reflect treatment-emergent adverse events, as defined in the introduction to the **ADVERSE REACTIONS** section, reported by the 1420 patients treated with Lexapro for periods of up to one year in double-blind or open-label clinical trials during its premarketing evaluation. All reported events are included except those already listed in Tables 2 & 3. Those occurring in only one patient, event terms that are so general as to be uninformative, and those that are unlikely to be drug related. It is important to emphasize that, although the events reported occurred during treatment with Lexapro, they were not necessarily caused by it. Events are further categorized by body system and listed in order of decreasing frequency according to the following definitions: frequent adverse events are those occurring on one or more occasions in at least 1/100 patients; cardiovascular - frequent palpitation, hypertension, infrequent: bradycardia, tachycardia, ECG abnormal, flushing, varicose vein, Central and Peripheral Nervous System Disorders - frequent: light-headed feeling, migraine, infrequent: tremor, vertigo, restless legs, shaking, twitching, dysequilibrium, tics, carpal tunnel syndrome, muscle contractions involuntary, sluggishness, coordination abnormal, faintness, hyperreflexia, muscular tone increased, Gastrointestinal Disorders - frequent: heartburn, abdominal cramp, gastroenteritis, infrequent: gastroesophageal reflux, bloating, abdominal discomfort, dyspepsia, increased stool frequency, belching, gastritis, hemorrhoids, gagging, polyposis gastric, swallowing difficult, General - frequent: allergy, pain in limb, fever, hot flashes, chest pain, infrequent: edema of extremities, chills, lightness of chest, leg pain, asthenia, syncope, malaise, anaphylaxis, fall, Hemic and Lymphatic Disorders - infrequent: bruise, anemia, nosebleed, hematoma, lymphadenopathy cervical, Metabolic and Nutritional Disorders - frequent: increased weight, infrequent: decreased weight, hyperglycemia, thirst, bilirubin increased, hepatic enzymes increased, gout, hypercholesterolemia, Musculoskeletal System Disorders - frequent: arthralgia, myalgia, infrequent: jaw stiffness, muscle cramp, muscle stiffness, arthritis, muscle weakness, back discomfort, arthropathy, jaw pain, joint stiffness, Psychiatric Disorders - frequent: appetite increased, lethargy, irritability, concentration impaired, infrequent: jitteriness, panic reaction, agitation, apathy, forgetfulness, depression aggravated, nervousness, restlessness aggravated, suicide attempt, amnesia, anxiety attack, bruxism, carbohydrate craving, confusion, depersonalization, disorientation, emotional lability, feeling unreal, tremulousness nervous, crying abnormal, depression, excitability, auditory hallucination, suicidal tendency, Reproductive Disorders/Female - frequent: menstrual cramps, menstrual disorder, infrequent: menorrhagia, breast neoplasm, pelvic inflammation, premenstrual syndrome, spotting between menses, \* based on female subjects only; N= 905 Respiratory System Disorders - frequent: bronchitis, sinus congestion, coughing, nasal congestion, sinus headache, infrequent: asthma, breath shortness, laryngitis, pneumonia, tracheitis, Skin and Appendages Disorders - frequent: rash, infrequent: pruritus, acne, alopecia, eczema, dermatitis, dry skin, folliculitis, lipoma, furunculosis, dry lips, skin nodules, Special Senses - frequent: vision blurred, tinnitus, infrequent: taste alteration, earache, conjunctivitis, vision abnormal, dry eyes, eye irritation, visual disturbance, eye infection, pupils dilated, metallic taste, Urinary System Disorders - frequent: urinary frequency, urinary tract infection, infrequent: urinary urgency, kidney stone, dysuria, blood in urine, **Events Reported Subsequent to the Marketing of Escitalopram** - Although no causal relationship to escitalopram treatment has been found, the following adverse events have been reported to have occurred in patients and to be temporally associated with escitalopram treatment during post-marketing experience and were not observed during the premarketing evaluation of escitalopram: abnormal gait, acute renal failure, aggression, akathisia, allergic reaction, anger, angioedema, atrial fibrillation, chorea-thetosis, delirium, delusion, diplopia, dysarthria, dyskinesia, dystonia, ecchymosis, erythema multiforme, extrapyramidal disorders, fulminant hepatitis, hepatic failure, hypoesthesia, hypoglycemia, hypokalemia, INR increased, gastrointestinal hemorrhage, glaucoma, grand mal seizures (or convulsions), hemolytic anemia, hepatic necrosis, hepatitis, hypotension, leucopenia, myocardial infarction, myoclonus, neuroleptic malignant syndrome, nightmare, nystagmus, orthostatic hypotension, pancreatitis, paranoia, photosensitivity reaction, priapism, prolactinemia, prothrombin decreased, pulmonary embolism, QT prolongation, rhabdomyolysis, seizures, serotonin syndrome, SIADH, spontaneous abortion, Stevens Johnson Syndrome, tardive dyskinesia, thrombocytopenia, thrombosis, torsade de pointes, toxic epidermal necrolysis, ventricular arrhythmia, ventricular tachycardia and visual hallucinations.

© 2007 Forest Laboratories, Inc.

Rev. 07/07

Licensed from H. Lundbeck A/S

## BMI's Association With Mortality Varies by Cause

BY ELIZABETH MEHCATIE

Senior Writer

A study using national health survey data has found varying associations between body mass index and mortality, depending on the cause.

Using data on cause-specific relative risks of mortality from the National Health and Nutrition Examination Survey (NHANES) from 1971-2002, Katherine M. Flegal, Ph.D., and colleagues looked at the association between body mass index (BMI) and excess deaths associated with three different BMI categories: underweight (BMI less than 18.5), overweight (BMI of 25 to less than 30), and obesity (BMI of 30 and over). Deaths were divided into three major categories: cardiovascular disease (CVD), cancer, and all other causes (noncancer, non-CVD causes). The normal-weight category was used as the reference group.

The underweight category was associated with significantly increased mortality from noncancer and non-CVD causes, but was not associated with increased cancer or CVD mortality.

The overweight category, however, was associated with significantly decreased mortality from noncancer and non-CVD causes. This category was not associated with cancer or CVD mortality, but was associated with significant increased mortality from diabetes and kidney disease. The net result was that the overweight category was associated with significantly decreased all-cause mortality overall, the authors reported.

The obese category was associated with significantly increased mortality from CVD, some cancers, and diabetes and kidney disease. There was no significant association between obesity and cancer mortality overall, or with noncancer, non-CVD mortality. But it was associated with increased mortality from obesity-related cancers such as colon, breast, esophageal, uterine, ovarian, kidney, and pancreatic cancer (JAMA 2007;298:2028-37).

These data "indicate that the associa-

tion of BMI with mortality varies considerably by cause of death," the authors concluded. These results also help clarify their findings in an earlier study, which found "excess overall mortality associated with underweight and obesity but not with overweight."

In an interview, Dr. Flegal, senior research scientist at the National Center for Health Statistics, Hyattsville, Md., and lead author of the study, said the study's results were similar to those in other studies and are not intended for clinical use. Instead, they are intended to make estimates of the contribution of obesity and overweight to excess deaths.

The current study is an extension of a study, published in 2005, which determined that, based on national survey data from 2000, all-cause mortality was significantly increased in the underweight and obese categories and significantly decreased in the overweight category when compared with normal-weight categories.

Dr. Flegal said although some media coverage of that study suggested the findings were unusual, the association of overweight with mortality that is similar to or lower than that for normal weight, as well as the idea that being overweight may offer some survival benefits, have been found in other studies.

She emphasized that the relationship between BMI and mortality is complex. The study is not "the arbiter of whether it's OK to be overweight or not."

Asked to comment on the study's findings, Dr. Jeffrey I. Mechanick said its implications could "easily and dangerously" be distorted and should not be interpreted to mean that the results support allowing oneself to remain overweight or that dieting to achieve a "normal" BMI may not be medically indicated. Overweight people are at risk for diseases associated with a higher morbidity and mortality rate, including diabetes, obesity, and metabolic syndrome, said Dr. Mechanick, director of metabolic support and clinical professor of medicine at Mount Sinai School of Medicine, New York. ■

## Long-Term Weight Loss Aids Arterial Flow, Function

**NEW ORLEANS** — Extremely obese individuals who lost weight and kept it off for at least 1 year significantly improved their vascular endothelial function, Dr. Noyan Gokce reported in a poster at the annual meeting of NAASO, the Obesity Society.

Arterial flow-mediated dilation rose by 3.2% in those who lost weight, but deteriorated by 1.1% in those whose weight increased or stayed the same, Dr. Gokce, a cardiologist at Boston Medical Center, said in an interview. Patients who lost weight also reduced their cholesterol and glucose levels.

Dr. Gokce and a colleague, recruited 39 consecutive subjects aged 34-58 years with a body mass index range of 36 kg/m<sup>2</sup> to 54 kg/m<sup>2</sup> who were seeking medical or surgical intervention for weight loss from the Nutrition and Weight Management Clinic at Boston Medical Center.

They measured the patients' arterial function, blood glucose, and cholesterol levels at baseline and at 12 months, and compared the results of those who lost weight with the results of those who gained weight or whose weight stayed the same. Of the total, 27 achieved successful weight loss, defined as a loss of at least 10% of body weight from baseline to 12-month follow-up, and 12 lost no weight or gained weight during the same period.

The weight-loss group showed a significant increase in flow-mediated dilation. At baseline, the mean flow-mediated dilation was impaired at 6.9% and 6.4% in weight-loss and no-weight-loss/weight-gain subjects, respectively. At 12 months, the mean flow-mediated dilation increased to 10.1% in weight-loss subjects and decreased slightly, to 5.3%, in the other group.

In addition, in those who lost weight, mean blood glucose decreased by 27 mg/dL, total cholesterol fell by 13 mg/dL, and mean triglyceride levels fell by 32 mg/dL. In those who gained or maintained their weight, mean blood glucose increased by 15 mg/dL, total cholesterol increased by 29 mg/dL, and mean triglyceride levels rose by 10 mg/dL.

—Fran Lowry